in the spinal canal under my observation, which owing to a misleading positive Wassermann reaction were treated with salvarsan, no deleterious results occurred, although the cases are too few to impart the confidence derivable from a larger number. Moreover, F. Epstein,[5] in the course of a discussion of the effects of salvarsan upon the eye, refers to the absence of nervous disturbances in the many patients who have been treated with salvarsan for malaria and other non-luetic diseases, and he quotes especially a report on 700 cases of framboesia tropica in which no mention is made of any injury to the nervous system.

To Dr. D'Arcy Power, of the San Francisco Polyclinic, I am indebted for his kindness in photographing the microscopic sections.

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# BANTI'S DISEASE AND ALLIED CONDITIONS.

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As a result of nearly thirty years' study, Banti,[1] a Florentine pathologist, recorded his investigations in a recent paper, summarizing his conclusions, previously published in various journals, as to the nature of the disease which bears his name. This disease, though not frequent, has called forth a deal of discussion; and any one who sets out to peruse the literature is at times bewildered if not totally discouraged, as pathologists, clinicians, and surgeons are sadly at variance as to the very existence, not to speak of the nosology, etiology, pathogenesis, and pathology of the disease. At the outset it may be stated that although it seems ill-advised to include under the name of Banti's disease any case which does not conform to the tenets set down by Banti himself, the impartial critic is bound to confess that any contribution to a subject in the making, like the one under discussion, is welcome if it is made with the requisite thoroughness of observation, so that its results may count in determining the status of a disease which, to say the least, it is difficult to delimit. It is to be deplored that many of the cases which are brought to bear on this subject are incompletely recorded, and that their pathological histology has received such scant attention. Since Osler[2] first drew the attention of the profession to the subject American and English clinicians have shown interest in the disease and its allied conditions.

Banti's disease is a primary splenomegaly of unknown origin;

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[5] Berlin. klin. Woch., 1911, xlviii, 2328.

[1] Folia Hæmatologica, Part I; Archiv. x, 33. See also Ziegler's Beiträge, 1898, Band iv, p. 21.

[2] Amer. Jour. Med. Sci., 1900, cxix, 54, and 1902, cxxiv, 751.

it is cryptogenetic, that is, not caused by syphilis, malaria, or leukemia. It is not a form of cirrhosis of the liver, as claimed by Naunyn, but a unique morbid entity, which shows: (1) Anemia of a characteristic though somewhat variable type; (2) cirrhosis of the liver which is identical with the ordinary Laennec's interlobular fibrous form and always is secondary to the splenomegaly; (3) ascites; (4) progressive hyposthenia, which invariably leads to a fatal issue; and (5) according to Senator[3] and Osler, it is not infrequently accompanied by severe or fatal hemorrhages from the nose, esophagus, stomach, or bowels. A low fever is sometimes observed.

In order to satisfy the practical demands of the clinician, Banti divides the disease into three stages: The first stage, which is marked by splenomegaly and anemia alone; the second stage, in which the enlarged cirrhotic liver becomes palpable; and the third, or ascitic stage. These three stages are subject to variations in length and intensity. The ascitic stage is terminal. Banti advises removal of the spleen before ascites sets in as the only means of curing this otherwise lethal constitutional affection.

What are the anatomical characteristics of Banti's disease? An extensive proliferation of the reticulum of the spleen, styled by its author fibroadenie. By this term he means to convey the fact that the lymphatic stroma of the pulp as well as that of a large number of the follicles, retains its reticular or adenomatous appearance. These changes take place primarily around the pencillated arterial system of the follicles, leaving the arterial walls intact. This pathological change is not characteristic of Banti's disease alone, but may be found in other diseases of the lymphatic system, as in leukemia. Although this process may be viewed in the light of a fibrosis, and is generally looked upon as such by pathologists, Banti lays stress on the proliferation of the lymphatic tissue of the pulp and the follicles in contradistinction to the ordinary (fibrous) proliferation of interstitial elastic or embryonal tissue. The changes in the liver are the well-known hypertrophy of the interlobular tissue, with secondary atrophy of the liver cells. Banti has taken particular pains to prove this, by probatory excisions and punctures of the liver. Naunyn[4] denies this; he claims that the hepatic changes are those of a primary lymphoid periportal infiltration. According to his view no evidence has been adduced to show that true cirrhosis of the liver develops from these interstitial changes.

Aside from the changes in the spleen and liver, there is often, though not invariably found, an endophlebitis of the splenic as well as the portal vein, at the point of entry of the former. In the third or ascitic stage of the disease, endophlebitis of the mesenteric veins is not uncommon.

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[3] Berl. klin. Woch., 1901, No. 46, and Deutsche Klinik, 1903, iii.

[4] Versammlung deutscher Naturforscher, Breslau, 1904.

It has been variously stated that Banti has classified the disease under discussion as an essential disease of the blood—as a disease of the hematopoietic organs. This is according to his own estimation of the condition, aside from the facts. Senator puts down leukopenia as a constant symptom. From the exhaustive hematological studies of Banti it is apparent that the leukopenia, though often observed, is not constant. The main blood changes are: (1) The number of erythrocytes is diminished; this is not constant, erythremia even being found in some cases; (2) the color index is lowered; (3) nucleated red cells and myelocytes are never present; (4) oligochromemia is always present; (5) leukopenia is present, though not invariably.

As regards the various forms of leukocytes: (1) There is an absolute or relative mononeucleosis; (2) there is an absolute or relative neutrophile leukopenia; (3) there is an absolute lymphocytic leukopenia.

The conclusions drawn by Banti are as follows: As the lymph nodes and bone marrow show nothing abnormal, there is on the one hand no evidence to prove that blood formation is impeded. Furthermore, as there is no urinobilinuria and no blood pigment in the spleen and the liver, there is nothing to show that there is an increased disintegration of the blood. It is, therefore, likely that the various elements of the blood are not thrown into the blood stream in sufficient quantities; there is also a possibility that they are retained in the hemopoietic organs.

What is the nosological relationship of Banti's disease in the medical system? According to Banti it belongs to the group of splenic anemias, or what is the same, primary splenomegalies of unknown etiology. He is inclined to assume two varieties of splenic anemias. The first or blood-disintegrating type of splenomegaly, in which the deleterious effect of the toxins formed in the spleen is principally exerted on the blood; in these cases the prosthenic symptoms predominate, and the patient dies from the effects of the severe anemia. In the second group, the toxins give rise to cirrhogenetic changes in the spleen and later in the liver. This latter group includes the Banti of three stages: Splenomegaly, cirrhosis of the liver, and ascites.

It should be added that in various communications aside from those of Banti, enlarged lymph nodes and embryonal bone marrow are noted, as also urinobilinuria. In his latest communication Banti states that endophlebitis of the portal root branches is not constant.

From this short review it can be seen that we are dealing here with a topic of extreme interest. This much can already be said: The various attempts to overthrow or to dissociate the pathological and clinical complex constructed by Banti have so far been unsuccessful, and the brilliant results obtained by surgical intervention will always stand. The various points in dispute, however, call for a closer study of the subject. A great deal is still to be learned as to the etiology, pathogenesis, and delimitation of Banti's disease from apparently similar groups of diseases. The whole subject, in fact, has assumed a new phase in the light of our recent advanced means of diagnosis of syphilitic disease. In order to bring out the various points at issue, it is of advantage to pass in critical review the principal work recorded in the literature of the subject.

THE TEACHINGS OF THE NAUNYN SCHOOL. As we have seen, Banti holds that the disease is a primary affection of the spleen, with secondary implication of the liver. This is a new departure in visceral pathology, for it always has been held that, aside from certain new formations of the spleen, whatever changes are found in that organ are secondary, and are caused by inflammatory conditions of those viscera, whose blood is gathered in the portal vein. This point is specially emphasized by Naunyn, who cannot agree with Banti in the interpretation of the disease. Splenomegaly with cirrhosis of the liver (Banti's disease) is, according to Naunyn, nothing more than a cirrhosis with the precirrhotic splenic tumor of Leichtenstern. Naunyn has seen cases with considerable splenic tumefaction (30 c.c. in length), anemia, ascites, and hemorrhages which are to him nothing more than forms of cirrhosis of the liver. He would relegate Banti's disease to that class of rare cases mentioned by Senator, in which ascites supervenes the splenomegaly, without the intermediate stage of cirrhosis.

Naunyn's attitude toward the whole question is upheld by Simmonds,[5] who states unequivocally that the diagnosis of Banti's disease cannot be made anatomically. The case recorded by Simmonds does not seem to have been studied with the completeness necessary to give sufficient ground for the sweeping statement quoted above; nor does it become clear from the short report, whether this author has observed cases of true Banti's disease.

The same criticism holds good for the observations including studies in metabolism of Umber[6] and of Brugsch.[7] Umber published a case which neither clinically nor pathologically is a true Banti. Starting from the original theory of Banti that the disease is caused by some toxin generated in the spleen, Umber determined the nitrogen balance and found evidence of toxigenic proteid disintegration. Splenectomy was done, whereupon all the symptoms disappeared, and the patient made a complete recovery. The metabolism was normal shortly after the operation. To prove the value of the metabolism test as an indication for splenectomy, Umber cites another case with hemoglobin of only 18 per cent., which seemed absolutely hopeless; fifteen punctures were done to relieve the ascites; exitus was daily expected. The nitrogen balance being normal, splenectomy was not attempted. All at once the patient improved rapidly, the ascites disappeared, and the erythrocytes were doubled in four months; but the size of the spleen remained the same. The subsequent history not being known, this improvement cannot be considered in the light of a cure. Brugsch follows closely the teachings of the above-named authors.

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[5] Aerztl. Verein in Hamburg, 1905.

[6] Zeitschr. f. klin. Med., 1904, Band lv.

[7] Mediz. Klinik, 1905, No. 23.

The teaching of Naunyn and his pupils may be summarized as follows: There is a form of cirrhosis of the liver which is accompanied by a considerable enlargement of the spleen. The interpretation put upon these cases by Banti as a primary splenomegaly cannot be upheld. Banti's disease (splenomegaly with ascites) is an extremely rare condition, which cannot be differentiated from cirrhosis with splenic engorgement. Anatomically, the diagnosis of Banti's disease is impossible to make. Splenectomy is indicated only when the toxigenic character of the case is demonstrated by the metabolic tests. Banti's disease may recover without operative interference.

THE HEMATOLOGICAL ASPECT OF BANTI'S DISEASE, AND ITS RELATION TO THE SPLENIC ANEMIAS. Banti is reserved in the interpretation of the blood changes, as well as in its classification in the medical system; he simply states that the affection probably represents one peculiar group of primary splenomegaly. According to Grawitz[8] it may be called a splenic pseudoleukemia, as it represents a primary adenomatous proliferation of the spleen. In this connection I would like to refer to an excellent study of Hultgen[9] who has constructed a short classification of the generalized primary affections of the hematopoietic system according to their essential hematology, and subdivided them according to their etiology and clinical course. Hultgen retains the name splenic anemias, a term first introduced by Griesinger, and later employed by continental authors, Osler, and others, but discarded by Naegeli.[10] Hultgen places Banti's disease under group *a* of his splenomegalies, that is, the group of unknown etiology, while under group *b* he places the splenic anemias of known etiology, such as the malarial, syphilitic, etc. To the latter group, in my opinion, should be appended the splenomegalies due to thrombophlebitis of the portal system. The conclusions reached by Hultgen will, for the present at least, suffice to answer the theory of Banti's disease in its hematological aspect, as variously discussed by Banti, Luce,[11] Naegeli, and others. To quote: "The question as to whether in splenic anemia the plastic or the lytic function of the spleen are individually or jointly involved cannot be settled as yet; but the study of blood counts of reds and total leukocytes taken from 82 cases in the literature, show distinctly parallel and synchronous movements. This I can interpret not as a sign of hematolysis, but as a slower bradyplastic hematopoiesis, as a disturbance of the entire blood-forming system."

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[8] Klinische Pathologie des Blutes.

[9] Jour. Amer. Med. Assoc., 1911, No. 4, p. 1526.

[10] Blutkrankheiten, 1908, p. 395.

[11] Mediz. Klinik, 1910, Nos. 14 and 15.

THROMBOPHLEBITIS OF THE PORTAL AND THE SPLENIC VEINS. As noted above, Banti mentions certain inflammatory changes in the veins of the portal system as a common though not constant feature of the disease. These changes are always secondary to the splenomegaly, and as the disease advances toward the ascitic stage the portal radicals also become affected. It is evident from these statements that endophlebitis of the portal has no direct bearing upon the etiology of the splenomegaly.

Since Banti's disease has become more generally known a number of authors have described phlebosclerosis and calcification of the portal veins in its pathological and clinical relationship to Banti's disease. A close perusal of the cases so far published undoubtedly shows that in phlebosclerosis of the portal vein and its branches we are dealing with a process etiologically and anatomically different from Banti's disease. As pointed out by Borrmann,[12] it is a process much like that of luetic disease of the aorta, although traumatism is repeatedly mentioned as a contributory etiological element. In a valuable study of this subject, which also includes the experimental side of the question, Warthin[13] lays particular stress on the part played by the phlebosclerosis of the portal veins, in producing a clinical picture so nearly identical with Banti's disease. "The whole pathological picture" of phlebosclerosis of the portal veins "points to an infective thrombophlebitis," "no matter under what head reported, splenic or portal thrombosis, splenic anemia or Banti's disease." If I do not misunderstand Warthin, he identifies all three conditions, as he considers them brought about by one cause—thrombophlebitis of the portal veins. This theory cannot hold, as long as there are cases of Banti's disease reported without the detailed affections of the veins of the portal system. As already mentioned, such cases have been reported by Banti, and although it may be true, as Warthin contends, that the examination of the portal veins at autopsy is not as complete as it should be, portal-vein obstruction is accompanied by such an abundant development of the collaterals that it cannot be easily overlooked. Primary splenomegaly with cirrhosis of the liver (Banti's disease) is an entity apart from thrombophlebitis of the portal vein.

THE RELATION OF SYPHILIS TO BANTI'S DISEASE. Banti in his original communication, as well as recently, positively denies, that syphilis is a factor in the etiology of the disease in question. Within recent years the whole subject of Banti's disease has been viewed with a great deal of interest from the fact that by reason of our improved diagnostic methods of syphilitic disease we are now enabled to substantiate the observations first made by Chiari[14] and Marchand,[15] that there is a disease which may be styled syphilitic Banti's disease, or syphilitic pseudo-Banti, which bears a remarkable relationship to the disease as originally described, both clinically and pathologically. This pseudotype is also, like the true Banti, a juvenile disease, is also characterized by enormous splenic tumefaction, enlargement of the liver, inflammatory changes of the vessels of the portal system, and blood changes similar to if not identical with those in Banti's disease—leukopenia and lymphemia. Gastric and enteric hemorrhages also occur. It is not surprising that, from the similarity of the two affections, attempts have been made to identify the syphilitic form with the original Banti's disease.

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[12] Archiv f. klin. Medizin, Band lix.

[13] International Clinics, 1910, twentieth series, p. 189.

Close study of the subject reveals the fact, however, that the pathology of the cases just referred to varies materially from that of Banti's disease in the syphilitic pseudotype, the main changes in spleen and liver begin and exhaust themselves in the vascular system of the affected organs. When the process is complete, it presents the fibrous deterioration of the vessels and tissues generally which is characteristic of visceral lues. Pathologically, the syphilitic type presents a true fibrosis; a proliferation of lymphatic tissue which is characteristic of Banti's disease is not apparent. In addition to this a case of true Banti with a positive Wassermann reaction has so far at least not been observed. However that may be, the fact remains that the syphilitic pseudo-Banti bears a close relationship to the disease as described by the original author.

Anyone who studies this subject critically would be led to infer that the proof of the existence of a condition so similar to Banti's disease would tend to throw some light on the perplexing problem of the etiology of the latter; and the question naturally arises in one's mind: Has not syphilis, after all, some direct bearing upon the etiology of Banti's disease? This must not be exclusively the case, if at all; may it not, possibly, develop on the basis of a devitalized organism of hereditary or acquired luetic taint, analogous to the condition known as arteriocapillary fibrosis or that which forms the basis of certain parasyphilitic systemic diseases of the nervous system? A more complete method of diagnosis of hereditary syphilis may shed some light on this subject. Therapeutically the luetic class of cases must be viewed apart by themselves.

From the above it is evident that there is still much to be learned before we arrive at a true interpretation of the disease under discussion. No earnest effort has, so far as I can see, been made, aside from the work of Banti himself, to enter into a thorough study of the histopathological basis of the disease, and we are bound to take Banti's work as the standard and accept the interpretation placed by that author upon the nature of the disease, its genesis, symptoms, and treatment. This standpoint, with certain limitations, will serve as a working basis from which the teachings of Banti can be extended. It lies in the nature of the disease, that a splenotoxic influence of the blood on the tissues, must be assumed as Banti did; to make this, however, the starting point of the whole question, has not proved satisfactory. The disturbance in metabolism noted in the thoroughly investigated case of Umber cannot be made the feature from which a differential diagnosis can be established, nor does the determination of the disturbed nitrogen balance before splenectomy bear upon the question of indication for that operation, in spite of the fact, that by this means, metabolic balance is restored. It would seem, that disturbed metabolism occurs in conditions allied to Banti's disease, and it is not unlikely, that disturbances of metabolism are but phases in the course of Banti's and similar constitutional diseases. It is safe to assume with Banti, Senator, Osler, and others, that in this disease we are dealing with a splenomegaly or splenic anemia of a peculiar type. From a broad clinical point of view it is furthermore evident, that it is above all a juvenile disease, bearing the earmarks of heredity or congenital disposition. As Luce has pointed out, it most frequently develops at the time of adolescence or shortly after, when the lymphatic structures of hereditary taint are most impressionable to various degenerative influences. With the conception of the disease, as a primary affection of the lymphatic structures of the spleen, the idea that cirrhosis of the liver is the underlying cause seems wholly improbable, although it must be granted, that clinically the differentiation of Banti's disease from certain cases of cirrhosis of the liver, with considerable splenic enlargement and severe anemia as described by Hoke[16] and Naunyn, must be difficult, if not impossible.

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[14] Präg. med. Woch., 1902, No. 21.

[15] Wien. med. Woch., 1902, No. 24.

A careful study of the recorded cases shows that the pathological delimitation of Banti's disease from other forms of splenomegaly and from apparently identical conditions, always assuming the Banti standard, is practicable. The Gaucher[17] type of splenomegaly is a distinct entity; considerable confusion is shown in the literature by confounding the two conditions. It should be stated here that there are certain carefully observed cases still unclassified which bear a relationship to the Gaucher type, and which have nothing in common with true Banti's disease.

In conclusion, the following may be said: Banti has formulated one group of splenomegalies, that which now bears his name, leaving for further research the grouping of other splenomegalies. The important factor of etiology he has left open. It is clearly the duty of other observers not to attempt to dissociate his symptom complex, nor to designate an allied symptom complex as Banti's disease, which differs intrinsically from that described by Banti.

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[16] Prag. med. Woch., 1899, Band xxiv, p. 451, and 1901, Band xxvi, p. 481.

[17] A. Borissowa, Virchow's Arch., 1903, Band clxxii, p. 108, and Stengel, AMER. JOUR. MED. SCI., 1904, clxxiii, 497.

THE CLINICAL ASPECT OF BANTI'S DISEASE. It is not the intention of the writer to discuss the differential diagnosis of Banti's disease from its allied conditions. The reader is referred to the excellent treatise by R. Hutchison and J. C. Ledingham,[18] for a summary clinical picture of the splenic anemias. Brill[19] holds that the Gaucher type can be distinguished clinically from other types or groups.

What seems most important to me is that for clinical purposes it is at present possible, first and foremost, to divide the splenic anemias into two groups: (1) The group with the positive Wassermann reaction, and (2) the group with the negative Wassermann reaction.[20] This classification will *eo ipso* determine the course of treatment, not losing sight of the fact that the Wassermann reaction may prove negative in cases of syphilis. I would propose that a provocative salvarsan injection (intravenous) be made in every case. Repeated treatment with salvarsan, together with the old-style energetic antispecific treatment, will always be in order as a tentative measure, especially in view of the fact that a certain group of cases is undoubtedly due to lues congenita tarda. Not too much, however, should be expected from the antiluetic treatment, as the disease, as shown by the fibrous organic changes, has already passed into the parasyphilitic stage, which is only in part (if at all) amenable to treatment and cure by means of the remedies at present at our command.

Finally, it should be stated that splenectomy has yielded excellent results,[21] and that the third or ascitic stage of the disease may now be successfully treated by the combination of splenectomy and the Talma operation. Altogether it is no exaggeration to state that the work of Banti stands today as one of the most brilliant achievements of medical science.

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[18] Splenic Anemias in Allbutt and Rolleston's System of Medicine, v, 757.

[19] Medical Record, March 2, 1912, p. 444.

[20] Neuberg, Zeitschr. f. klin. Med., 1911, p. 92, and Ridder, Charité Annalen, 35 Jahrgang, p. 193.

[21] According to Rehling, 8 per cent. mortality in 70 cases; see Festschrift des deutscher Hospitals, New York, 1909, p. 320. Rehling transfused before operation.